Hyperlipidemia

Prepared for Kansas Medical Assistance Program in December, 2004

EXECUTIVE SUMMARY

Purpose of Intervention

The purpose of this intervention is to identify opportunities for improving coronary heart disease (CHD) prevention with lifestyle modifications and lipid lowering drug therapies following NCEP guidelines.

Intervention

Intervention Type	Population-based mailing
Intervention Mailing Date	February 2004
Pre-intervention Period (Baseline)	September 2003 – February 2004
Post-intervention Period (Post)	April 2004 – September 2004
Number of Letters Mailed	1,636
Number of Targeted Physicians	1,636
Number of Targeted Patients	6,866
Adjusted Targeted Patients	4,813
Number of Control Physicians	0
Number of Control Patients	0
Adjusted Control Patients	0

Changes in Clinical Indicators

Clinical Indicators	Target		
	Baseline	Sep-04	% Change
Drug-Drug Interactions	**48**	**40**	**-16.7%**
Underutilization	**4,622**	**3,489**	**-24.5%**
Increased Risk of ADE	**5**	**4**	**-20.0%**
Non-Compliance	**139**	**44**	**-68.3%**

BACKGROUND

Coronary heart disease (CHD) is the leading cause of death in the US afflicting more than 13 million patients, thus it imposes a major burden on society in terms of morbidity, mortality, and economic costs. According to the 2004 Heart and Stroke Statistics, the total (direct and indirect) cost of care for CHD in 2004 is estimated to be $133 billion. Of the total direct costs, hospital and nursing home costs account for $43.7 billion and drugs/other medical durables for $8.5 billion.[1]

Elevated cholesterol is a known risk factor for CHD. Lowering cholesterol slows the progression of coronary artery lesions and decreases coronary event rates.[2] Recent clinical trials have demonstrated reductions in morbidity and mortality with LDL lowering therapy, in particular with HMG-CoA reductase (statins) inhibitors.[3-10] The National Cholesterol Education Program (NCEP) was formed in 1985 and subsequently released the first cholesterol treatment guidelines in 1988. The NCEP is an effort to increase awareness of the dangers of high cholesterol levels and the benefits of reducing cholesterol levels. The treatment guidelines provided by the NCEP aid clinicians in making decisions regarding cholesterol monitoring and therapy initiation, thereby reducing the risk of CHD. The expert panel from this program released its most recent report, the NCEP-Adult Treatment Panel (ATP) III, in May 2001.[2] The ATP III provides new guidelines for assessment of CHD risk and continues to emphasize LDL cholesterol as the primary target of therapy.

A 2004 update to the NCEP clinical practice guidelines suggests a more aggressive therapeutic option (LDL cholesterol < 70 mg/dL) for patients at very high risk for CHD based on recent clinical trials. Factors that place patients at very high risk include:[11]

- The presence of established CVD plus (1) multiple major risk factors (especially diabetes)
- Severe and poorly controlled risk factors (especially continued cigarette smoking)
- Multiple risk factors of the metabolic syndrome (especially high triglycerides ≥200 mg/dL plus non-HDL-C ≥130 mg/dL with low HDL-C of ≤ 40 mg/dL], and
- On the basis of PROVE IT[10], patients with acute coronary syndromes

[1] American Heart Association. Heart Disease and Stroke Statistics — 2004 Update. Dallas, Tex.: American Heart Association; 2003. Also available from http://www.americanheart.org/presenter.jhtml?identifier=1928.

[2] National Cholesterol Education Program. Third report of the Expert Panel on Detection, Evaluation, and Treatment of High Cholesterol in Adults (Adult Treatment Panel III).JAMA 2001;285:2486-2497.

[3] Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia: West of Scotland Coronary Prevention Study Group. N Engl J Med 1995; 333: 1301-1307.

[4] Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: Results of AFCAPS/TexCAPS-Air Force/Texas Coronary Atherosclerosis Prevention Study. JAMA 1998; 279: 1615-1622.

[5] Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: The Scandinavian Simvastatin Survival Study (4S). Lancet 1994; 344: 1383-1389.

[6] Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, Cole TG, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels: Cholesterol and Recurrent Events Trial Investigators. N Engl J Med 1996; 335: 1001-1009.

[7] The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998; 339: 1349-1357.

[8] Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: A randomised placebo-controlled trial. Lancet 2002; 360: 7-22.

[9] Sever PS, Dahlöf B, Poulter NR, et al., for the ASCOT investigators. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower that average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA): a multicenter randomized controlled trial. Lancet 2003; 361: 1149-1158.

[10] The Pravastatin or Atorvastatin Evaluation and Infection Therapy – Thrombolysis in Myocardial Infarction 22 Investigators, Cannon CP, Eugene Braunwald E, McCabe CH, et al. Comparison of intensive and moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med 2004; 350.

[11] NCEP Report. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panell III Guidelines. Circulation 2004; 110:227-239.

Despite the information from recent trials and the NCEP guidelines, hyperlipidemia is often untreated or undertreated. National estimates indicate that only 35% of primary prevention patients needing therapy are receiving it.[12] In 2001, 59% of patients enrolled in commercial managed care plans and hospitalized for heart attack, bypass surgery, or angioplasty were treated to an LDL cholesterol goal of less than 130 mg/dL This proportion represented an increase from 45% from 1999. If all practices performed at the 90th percentile level (72%), 4,700 deaths could be avoided each year. In comparison, for 2000 the Medicaid rate for reaching an LDL cholesterol goal of less than 130 mg/dL was 28%, the Medicare rate was 53%, and the commercial rate was 53%. The 2001 NCEP ATP III guidelines recommend a more aggressive goal of less than 100 mg/dL. With this in mind, the treatment rates are likely much worse than suggested.[1]

When targeting patients at greatest risk for having a CHD event, lipid lowering therapy has been shown to be cost effective. The average costs of a coronary artery bypass graft (CABG) and percutaneous transluminal coronary angioplasty (PTCA) in 2001 were $60,853 and $28,558, respectively.[3] Studies have shown that if cholesterol levels can be lowered in high risk patients, the costs to treat CHD complications can potentially be avoided.[13]

[12] Hoerger TJ, et al. Treatment patterns and distribution of low-density lipoprotein cholesterol levels in treatment-eligible United States adults. Am J Cardiol 1998; 82:61-65.

[13] McKenney JM, Knosian B. Economic benefits of aggressive lipid lowering: a managed care perspective. Am J Man Care 1998;4:65-74.

METHODOLOGY

Changes in prescribing habits for intervention-related drugs were examined. This intervention identified providers whose patients were affected by potential drug-drug interactions, underutilization of therapy, increased risk of adverse drug events, or non-compliance with drug therapy. To assess the impact of the intervention, pharmacy drug claims were reviewed from April 2004 through September 2004.

Clinical Criteria: Criteria, rationale, and text message(s) to providers are listed below. All physicians with at least one recipient "hitting" on criteria received letters.

- Drug-Drug Interaction
  This indicator identifies patients receiving a lipid lowering medication and concomitantly receiving an interacting drug.

  Rationale: Patients with potential drug-drug interactions are at increased risk of having an adverse drug event. There may be coordination of care issues if more than one prescriber is involved.

  Sample Provider Paragraph:

  > Lovastatin - Warfarin: Lovastatin may increase the hypoprothrombinemic effect of warfarin. Please consider an alternative or monitor the prothrombin time (PT) or international normalized ratio (INR) when the combination is prescribed, especially when changes in lovastatin therapy are made.

- Underutilization
  The underutilization of therapy indicator identifies patients with a history of CHD or CHD risk equivalents as determined by diagnoses, procedures or drug use, or with risk factors placing them at moderate to high risk for developing CHD.

  Rationale: Clinical studies have shown the benefits of lipid lowering agents, particularly HMG-CoA reductase inhibitors, in patients with coronary heart disease, as well as patients with borderline cholesterol levels and no clinically evident disease. As stated above, there are large groups of patients who are either not treated or under treated.

  Sample Provider Paragraph:

  > Potential underutilization of lipid lowering therapy (primary prevention): According to submitted diagnosis and/or pharmacy claim data, it appears that your patient has 2 or more risk factors (i.e., age, hypertension, smoking history) for CHD and is not receiving pharmacological lipid lowering therapy. According to the National Cholesterol Education Program (NCEP) guidelines, patients with a history of 2 or more risk factors should maintain LDL cholesterol <= 130mg/dL. Please review your records to determine if a lipid panel has been checked recently (i.e., in the past year) and evaluate the potential need for lipid lowering therapy (diet and pharmacological).

- Increased Risk of Adverse Drug Events
  The increased risk of adverse drug event indicator identifies patients receiving nicotinic acid with a history of diabetes, gout or peptic ulcer disease, a HMG CoA inhibitor with a history of liver dysfunction, myopathy or current pregnancy, or fibrate with a history of hepatic or renal dysfunction, primary biliary cirrhosis or current pregnancy.

Rationale: Patients with potential drug-disease interactions are at an increased risk of having an adverse drug event.

Sample Provider Paragraph:

> Increased risk of adverse effect: Niacin use in gout patients. According to submitted diagnosis and/or pharmacy claim data, it appears that your patient has gout and recently received niacin. Niacin can cause hyperuricemia which can worsen gout. Please consider if an alternative antilipemic agent is appropriate or monitor for signs and symptoms of hyperuricemia.

- Medication Non-Compliance

  Patients receiving lipid lowering therapy who received less than 60 days supply of the drug during a 90-day period of time.

  Rationale: Compliance with prescribed maintenance drug regimens is paramount to successful patient outcomes. More than $100 billion is spent yearly for problems related to noncompliance. Over half of written prescriptions are taken incorrectly.[14]

  Sample Provider Paragraph:

  > Your patient may be non-compliant with the identified chronic antilipemic therapy. From prescription data, it appears that your patient received <60 days of maintenance therapy in a 90 day period. Please review this information to determine the best course of action for your patient.

Definitions:

Adjusted Target Patients – All patients of physicians who were included in the intervention, who had pharmacy claims and were active plan members throughout the post-intervention time period. Additionally, when outcomes are performed, these patients' pre-intervention (baseline) hits are re-evaluated to make certain that the status of clinical indicators haven't changed for each patient due to late pharmacy and medical claims.

Intervention-Related Drugs – antilipemics.

[14] Berg JS et al. Medication compliance: a healthcare problem. Ann Pharmacother 1993;27(suppl 9): S1-S24.

RESULTS

Characteristics

Table 1 describes the patient population included in the population-based intervention based upon mean age, gender, number of providers, average number of prescriptions per patient per month, and utilization of intervention-related drugs at baseline. As can be seen from the table, the target group had about twice as many females as males, were seeing 4.3 providers, receiving 7.2 prescriptions per month, and taking very few intervention-related drugs.

Table 1: Patient Characteristics

	Target (N=4,813)
Mean Age	62.5
Percentage Male	34.4%
Percentage Female	65.6%
Number of Providers	4.3
Average Number of Prescriptions PPPM*	7.2
Utilization of Intervention-Related Drugs**	
Average Number of Drugs***	0.0
Average Number of Claims	0.2
Average Days Supply	4.6
Average Amount Paid	$13.50

* Number of prescriptions per patient per month (PPPM) is the average for the 6 month baseline period

** Based on 6 months of baseline claims data

*** A distinct drug is defined by using a coding system similar to the Hierarchical Ingredient Code List (HICL) in that distinct drugs are identified at the ingredient level.

Drug-Drug Interactions

Table 2 exhibits the incidence of patients identified as being at risk for potential drug-drug interactions. The intervention saw reductions in half of the indicators. Overall, a reduction in drug-drug interaction clinical indicators of 16.7% was achieved during the post-intervention period.

Table 2: Changes in Drug-Drug Interactions

Drug-Drug Interactions	Target		
	Baseline	Sep-04	% Change
Lovastatin-Warfarin	2	1	-50.0%
HMG-Nefazodone	2	2	0.0%
Gemfibrozil-Warfarin	1	1	0.0%
Fenofibate-Warfarin	3	2	-33.3%
HMG COA Reductase Inhibitors-Phenytoin	7	7	0.0%
HMG COA Reductase Inhibitors-CCB	27	23	-14.8%
HMG-Macrolides	2	1	-50.0%
Cholestyramine-Thyroid Hormone	2	2	0.0%
Cholestyramine-Valproic Acid	1	1	0.0%
Bile Acid Sequestrants-Furosemide	1	0	-100.0%
Total	48	40	-16.7%

Underutilization

Table 3 presents the incidence of patients identified as underutilizing lipid lowering therapy and antilipemic therapy. Overall, a reduction in underutilization clinical indicators of 24.5% was achieved during the post-intervention period.

Table 3: Changes in Underutilization

Underutilization	Target		
	Baseline	Sep-04	% Change
Lipid lowering therapy [primary prevention]	1,092	782	-28.4%
Lipid lowering therapy [2nd prevention]	3,297	2,692	-18.4%
Antilipemic Therapy (primary prevention)	32	1	-96.9%
Antilipemic Therapy (secondary prevention)	201	14	-93.0%
Total	4,622	3,489	-24.5%

Increased Risk of ADE

The change in the number of patients identified as being at an increased risk of ADE is presented in Table 4. Overall, a reduction in the increased risk of ADE clinical indicators of 20.0% was achieved during the post-intervention period.

Table 4: Changes in Risk of ADE

Increased Risk of ADE	Target		
	Baseline	Sep-04	% Change
Niacin use in gout patients	1	1	0.0%
Fibrate & Renal Dysfunction	4	3	-25.0%
Total	5	4	-20.0%

Non-Compliance

Table 5 exhibits the changes in the number of patients identified as being non-compliant with their drug therapy. The intervention saw a sizable reduction in the antilipemics indicator. Overall, a reduction in non-compliance clinical indicators of 68.3% was achieved during the post-intervention period.

Table 5: Changes in Non-Compliance

Non-Compliance	Target		
	Baseline	Sep-04	% Change
Antilipemics	139	44	-68.3%

LIMITATIONS

A control group was not utilized for this intervention. This limited the comparisons that could be performed in the analysis. Therefore, instead of being able to compare an intervention group with a non-intervention group, the analysis is essentially limited to changes in the intervention group before and after intervention.

The time frame of 6 months may not capture the full extent of the impact of the hyperlipidemia intervention. Providers may be required some time before they can change their patient's drug regimens.

CONCLUSIONS

This hyperlipidemia intervention focused on improving coronary heart disease (CHD) prevention with lifestyle modifications and lipid lowering drug therapies. The intervention identified providers whose patients were affected by potential drug-drug interactions, underutilization of therapy, increased risk of adverse drug events (ADE) and non-compliance with drug therapy.

The intervention was successful in reducing the target patients flagged for each of the clinical indicator classes.

- Drug-Drug Interactions – Patients receiving a lipid lowering medication and concomitantly receiving an interacting drug saw a decrease of 16.7%.

- Underutilization – Patients with a history of CHD or CHD risk equivalents as determined by diagnosis, procedures or drug use, or patients with risk factors placing them at moderate to high risk for developing CHD were reduced by 24.5%.

- Increased Risk of ADE – Patients receiving nicotinic acid with a history of diabetes, gout or peptic ulcer disease, a HMG CoA inhibitor with a history of liver dysfunction, myopathy or current pregnancy, or fibrates with a history of hepatic or renal dysfunction, primary biliary cirrhosis or current pregnancy saw a reduction of 20.0%.

- Non-Compliance – Patients receiving lipid lowering therapy who received less than 60 days supply of the drug during a 90-day period of time saw a 68.3% reduction in non-compliance.